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Health and Environmental Effects Profile for Bromochloroethanes

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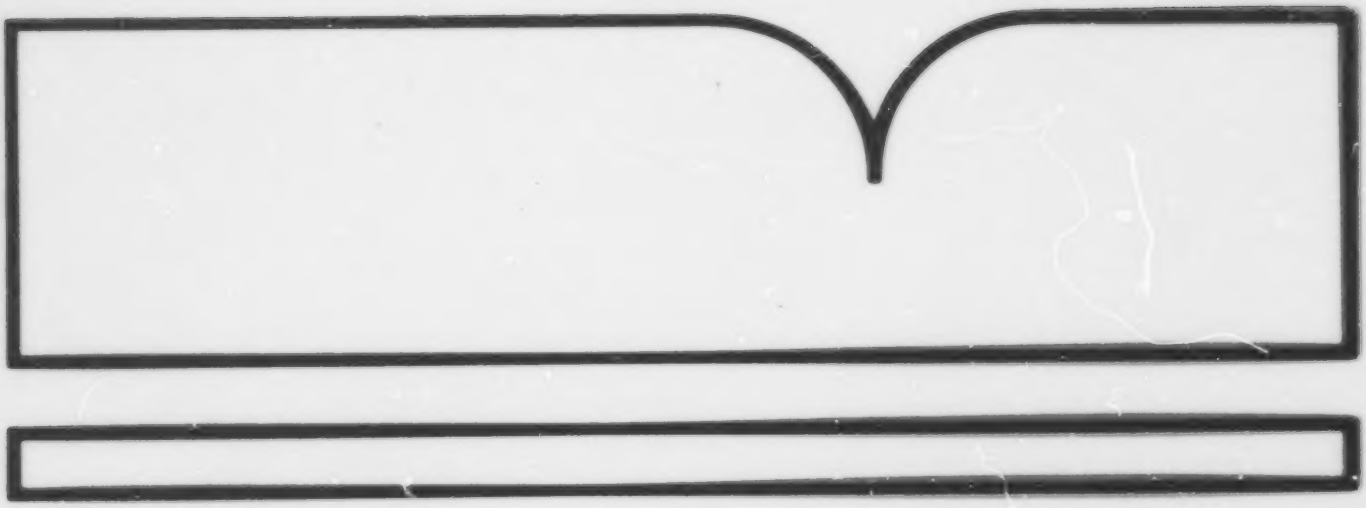

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR BROMOCHLOROETHANES

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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16. ABSTRACT

The Health and Environmental Effects Profile for bromochloroethanes was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Existing data are insufficient to determine an Acceptable Daily Intake (ADI) or a carcinogenic potency factor for bromochloroethanes.

The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a relase as specified by CERCLA based on chronic toxicity. Existing data are insufficient to determine an RQ value.

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste and Emergency Response by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA), as well as to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched." The literature search material is current through November, 1984.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor of q_1^* (U.S. EPA, 1980) is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity and acute mammalian toxicity).

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA and CERCLA dockets.

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LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
BUN	Blood urea nitrogen
CAS	Chemical Abstracts Service
CHO	Chinese hamster ovary
CNS	Central nervous system
DNA	Deoxyribonucleic acid
GC/MS	Gas chromatography/mass spectrometry
GSH	Reduced glutathione
HGPRT	Hypoxanthine-quinine phosphoribosyl transferase
KCN	Potassium cyanide
K_{oc}	Soil sorption coefficient
LC_{50}	Concentration lethal to 50% of recipients
LD_{50}	Dose lethal to 50% of recipients
NADH	Nicotinamide adenine dinucleotide (reduced form)
NADPH	Nicotinamide adenine dinucleotide phosphate (reduced form)
ppb	Parts per billion
ppm	Parts per million
ppt	Parts per trillion
RNA	Ribonucleic acid
RQ	Reportable quantity
SGPT	Serum glutamic pyruvic transaminase
WS	Water solubility

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

The structures, CAS Registry numbers, molecular weights and empirical formulas of a few bromochloroethanes are presented in Table 1-1. Of the bromochloroethanes listed in Table 1-1, useful chemical and biological data are predominantly limited to only one compound, 1-bromo-2-chloroethane, which is also known by the synonyms ethylene chlorobromide, sym-bromochloroethane, s-chlorobromoethane, 2-bromoethyl chloride and 2-chloroethyl bromide.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

1-Bromo-2-chloroethane is a colorless, volatile liquid with a chloroform-like odor (Hawley, 1977). Some of its relevant physical properties are listed below:

Melting point:	-16.5°C (Stenger, 1978)
Boiling point:	106.8°C (Stenger, 1978)
Density, 20/4°C:	1.7392 (Stenger, 1978)
Refractive index, at 20°C:	1.4917 (Stenger, 1978)
Water solubility, at 30°C:	0.7 g/100 mL (Metcalf, 1981) 0.69 parts/100 parts water (Perry and Chilton, 1973)
Vapor pressure, mm Hg:	
at 20°C	39.8 (Metcalf, 1981)
at 4.1°C	10 (Perry and Chilton, 1973)
at 16°C	20 (Perry and Chilton, 1973)
at 29.7°C	40 (Perry and Chilton, 1973)

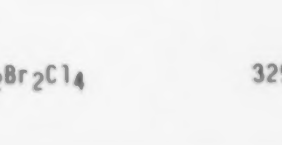
1-Bromo-2-chloroethane is soluble in alcohol and ether and is nonflammable (Hawley, 1977).

TABLE 1-1

Structures, CAS Numbers, Molecular Weights
and Empirical Formulas of Bromochloroethanes

Bromochloroethanes	CAS Number	Empirical Formula	Molecular Weight	Structure
1-Bromo-2-chloroethane	107-04-0	C_2H_4BrCl	143.42	
1-Bromo-1-chloroethane	593-96-4	C_2H_4BrCl	143.42	
2-Bromo-1,1-dichloroethane	683-53-4	$C_2H_3BrCl_2$	177.8	
1,2-Dibromo-1-chloroethane	598-20-9	$C_2H_3Br_2Cl$	222.3	

TABLE 1-1 (cont.)

Bromochloroethanes	CAS Number	Empirical Formula	Molecular Weight	Structure
1,2-Dibromo-1,2-dichloroethane	683-68-1	$C_2H_2Br_2Cl_2$	256.8	
1,2-Dibromo-1,1-dichloroethane	75-81-0	$C_2H_2Br_2Cl_2$	256.8	
1,1-Dibromo-1,2,2,2-tetrachloroethane	630-24-0	$C_2Br_2Cl_4$	325.6	

The available physical properties for 1-bromo-1-chloroethane are as follows (Perry and Chilton, 1973):

Melting point:	16.6°C
Vapor pressure, mm Hg:	
at 0°C	20
at 17°C	60
at 28°C	100

Useful physical or chemical properties of other bromochloroethanes were not located in the available literature cited in the Appendix.

1.3. PRODUCTION DATA

Production information concerning the bromochloroethanes, as provided by the U.S. EPA (1977), is available only for 1-bromo-2-chloroethane. The U.S. EPA (1977) lists the following data for 1-bromo-2-chloroethane:

Eastman Kodak, Rochester, NY	zero production in 1977
Ameribrom, Inc., NY, NY	imported an undisclosed quantity in 1977

No data in the available literature, including SRI (1984) and USITC (1983), indicate that 1-bromo-2-chloroethane or any other bromochloroethane is currently being produced domestically in commercially significant amounts; domestic production may be limited to laboratory reagents. 1-Bromo-2-chloroethane is prepared by reacting ethylene gas with bromine and chlorine (Hawley, 1977); some dibromo and dichloro compounds will be formed at the same time (Stenger, 1978). Current importation figures are not available.

1.4. USE DATA

1-Bromo-2-chloroethane has been used as an insecticidal fumigant for soils, commodities, fruits and vegetables (Worthing and Walker, 1983;

Hawley, 1977; Metcalf, 1981); however, there is currently little commercial interest in the fumigant use of 1-bromo-2-chloroethane (Worthing and Walker, 1983). 1-Bromo-2-chloroethane can also be used as a solvent, especially for cellulose esters and ethers, and as an intermediate in organic synthesis (Stenger, 1978; Hawley, 1977).

Use data for other bromochloroethanes were not located in the available literature cited in the Appendix.

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

The fate of bromochloroethanes in the environment will depend upon their ability to undergo chemical, photochemical and biological reactions and their ability to transport (partition) from one environmental matrix (water, air, sediment-soil) to another. Studies that directly examine the environmental fate and transport processes of the bromochloroethanes were not located in the available literature. Physical properties useful in predicting various transport processes are available for 1-bromo-2-chloroethane.

2.1. WATER

Based on structure activity relationships, hydrolysis is not expected to be an important determinant in the fate of the bromochloroethanes in water. Photolysis and microbial degradation data are not available.

Transport of the bromochloroethanes in the aquatic environment will depend upon the ability of the compounds to volatilize, to absorb to particulate organic matter or to bioaccumulate in aquatic organisms. Using available water solubility and vapor pressure data for 1-bromo-2-chloroethane, a Henry's Law constant is calculated to be of the order of 10^{-3}(atm-m^3/mol). This value indicates that volatilization of 1-bromo-2-chloroethane from water is both rapid and significant.

The K_{oc} and BCF can be estimated from the following equations presented by Kenaga (1980):

$$\log K_{oc} = 3.64-0.55\ (\log WS)\pm 1.23 \text{ orders of magnitude (95\% confidence limit)} \quad (2\text{-}1)$$

$$\log BCF = 2.791-0.564\ (\log WS)\pm 1.99 \text{ orders of magnitude (95\% confidence limit)} \quad (2\text{-}2)$$

where WS is water solubility in ppm. For 1-bromo-2-chloroethane, the K_{oc} and BCF values are ~34 and 4, respectively. These values indicate that

1-bromo-2-chloroethane is not significantly absorbed by particulate matter in water and is not likely to bioaccumulate significantly in aquatic organisms. Therefore, based on physical property estimations, volatilization is a predominant fate and transport mechanism in water.

2.2. AIR

Pertinent data specifically considering the chemical removal processes for bromochloroethanes from the atmosphere were not located in the available literature. The chemical removal processes include reaction with hydroxyl radicals, ozone and other radicals and photolytic transformations. Rate constants for the reaction of the bromochloroethanes with OH radicals are not available. Rate constants are available, however, for both 1,2-dichloro- and 1,2-dibromoethane. Singh et al. (1981) estimated the atmospheric residence times for these compounds to be 53 and 46 days, respectively. Therefore, 1-bromo-2-chloroethane is likely to have an atmospheric residence time of ~50 days. The loss of bromochloroethane through atmospheric ozone reaction is not likely to be important (Lyman et al., 1982). No photolysis data are available.

Based on the physical properties of bromochloroethanes, the atmospheric physical removal processes (dissolution, adsorption and deposition) are not likely to be important.

2.3. SOIL

Pertinent data regarding chemical, microbial or photochemical alterations of bromochloroethanes in soil were not located in the available literature cited in the Appendix.

The relatively high vapor pressure of 1-bromo-2-chloroethane indicates that it will evaporate rapidly from dry soil surfaces. Under dry conditions, volatilization is likely to be the predominant environmental fate

mechansim. In wet soils, this result is not as clear, although the information presented in Section 2.1. suggests that volatilization from aquatic environments is rapid. Also, the K_{oc} for 1-bromo-2-chloroethane can be calculated to be ~34 (see Section 2.1.). This value indicates that 1-bromo-2-chloroethane is not tightly bound in soil and is, therefore, likely to be leached from soils. Experimental adsorption data for soil were not available.

3. EXPOSURE

3.1. WATER

Ewing et al. (1977) collected surface water samples from 204 sites near heavily industrialized areas across the United States and analyzed the samples for contaminants present at concentrations >1 ppb. Organic contaminants were identified by GC/MS. The following bromochloroethanes were detected in the 204 samples at the following frequencies:

	Frequency of Detection
1-bromo-2-chloroethane	1
1-bromo-1-chloroethane	2
bromodichloroethane	2
dibromochloroethane	1

Decarlo (1979) examined water, air and sediment samples surrounding the bromine industry in El Dorado and Magnolia, Arkansas to identify the brominated chemicals present in the environment. Samples were taken at the major chemical facilities and in the neighboring environment. 1-Bromo-2-chloroethane was detected in water, air and sediment matrices; however, frequencies of detection and concentrations were not given.

The U.S. EPA STORET Data Base contained six observations of 1-bromo-2-chloroethane in water samples and three observations of 1-bromo-2-chloroethane in sediment samples. The concentration in five water samples was reported as 5 µg/ℓ, while the sixth water sample had a reported concentration of 2 µg/ℓ. The concentration of 1-bromo-2-chloroethane in all three sediments was reported as 5 µg/kg. No monitoring data for other bromochloroethanes was available from STORET.

Pellizzari et al. (1979) reported that two water samples in the New Jersey area contained bromodichloroethane at concentrations of 5.0 µg/ℓ.

The formation of bromochloroethanes in water supplies resulting from chlorination of water has not been reported in the literature. While the widespread formation of bromochloromethanes in chlorinated water has been reported (Trussell and Umphres, 1978), there is no current available evidence suggesting similar formation of bromochloroethanes.

3.2. FOOD

Using laboratory conditions, Seo et al. (1970) examined various Hawaiian fruits and vegetables for residues resulting from fumigation with 1-bromo-2-chlorcethane. Fumigation was accomplished by packaging the fruit or vegetables in cartons and then subjecting the food products to minimum required dose levels of 24 mg/ℓ for 2 hours. Dose levels of 48 mg/ℓ were also tested. Using ambient storage temperatures (21.1-26.7°C) on packaged bell peppers, residues of 1-bromo-2-chloroethane were not detectable 3 days post-treatment; residues 1 day post-treatment were 6.2 ppm at the dose level of 24 mg/ℓ and 11.1 ppm at the dose level of 48 mg/ℓ. Using a colder storage temperature (6.1°C) and a 24 mg/ℓ dose level, 1-bromo-2-chloro-ethane residues were 3.0 ppm 1 day post-treatment, and 1.0 ppm 3 days post-treatment.

3.3. INHALATION

Brodzinsky and Singh (1982) collected and collated ambient air monitoring data generated by 241 reference sources covering 151 chemicals. Available data for 1-bromo-2-chloroethane are summarized in Table 3-1. With the exception of Grand Canyon, AZ, monitoring was done in source areas such as bromine-chemical manufacturing facilities or use areas. As noted in

TABLE 3-1

Ambient Air Detections and Concentrations of 1-Bromo-2-Chloroethane*

Location	NPTS	NZER	Mean Concentration (ppt)	Maximum Concentration Detected (ppt)
Edison, NJ	13	9	880	1100
El Dorado, AR	35	18	61	760
Magnolia, AR	28	21	16	44
Grand Canyon, AZ	7	7	0	0

*Source: Brodzinsky and Singh, 1982

NPTS = number of data points for the location

NZER = number of data points below detection limits

Section 3.1., DeCarlo (1979) also reported the detection of 1-bromo-2-chloroethane in the ambient air near bromine facilities in Magnolia and El Dorado, AR.

3.4. DERMAL

Pertinent data regarding dermal monitoring of bromochloroethanes were not located in the available literature cited in the Appendix.

4. PHARMACOKINETICS

4.1. ABSORPTION

Pertinent data regarding the absorption of bromochloroethanes were not located in the available literature cited in the Appendix.

4.2. DISTRIBUTION

Pertinent data regarding the distribution of bromochloroethanes were not located in the available literature cited in the Appendix.

4.3. METABOLISM

According to van Bladeren et al. (1981), GSH conjugation with halogenated hydrocarbons is catalyzed by the cytosolic GSH transferases. The sulfur atom from GSH becomes attached to the carbon atom, displacing a halogen atom. If a vicinal halogen atom is present on the adjacent carbon, a reactive 2-halogenothioether results (Baganz and Dransch, 1960).

4.4. EXCRETION

Pertinent data regarding the excretion of bromochloroethanes were not located in the available literature cited in the Appendix.

5. EFFECTS

5.1. CARCINOGENICITY

No studies of the potential carcinogenicity of the bromochloroethanes per se were located in the available literature cited in the Appendix, and these chemicals are not scheduled for testing by the National Toxicology Program (NTP, 1984).

Structurally related haloalkanes, such as 1,1- and 1,2-dichloroethanes, 1,2-dibromoethane and 1,2-dibromo-3-chloropropane, have been tested for carcinogenicity by the NTP (1984). Haloalkane administration to rodents has been associated with the induction of hepatic tumors, upper respiratory and nasal cavity adenomas and carcinomas when administered by inhalation, and squamous cell carcinomas of the forestomach when administered orally (IARC, 1979).

5.2. MUTAGENICITY

The only bromochloroethane for which mutagenicity studies were available is 1-bromo-2-chloroethane. Details of these studies are summarized in Table 5-1. 1-Bromo-2-chloroethane was positive for reverse mutation in Salmonella typhimurium strains TA1530, TA1535 and TA100, but not in TA1538, when tested in the absence of the S-9 fraction from rat liver homogenates (Brem et al., 1974). The mutagenic response was not enhanced in strains TA100 and TA1535 in the presence of S-9, and the 1-bromo-2-chloroethane was negative in TA98, both with and without S-9 (Barber et al., 1981). The importance of the GSH-transferase-catalyzed conjugation of 1-bromo-2-chloroethane with GSH in the expression of the mutagenic response of the compound was investigated by

TABLE 5-1

Mutagenicity and Genotoxicity Testing of 1-Bromo-2-Chloroethane

Assay	Indicator/ Organism	Purity	Application	Concentration or Dose	Activating System	Response	Comment	Reference
Reverse mutation	Salmonella typhimurium TA1530 TA1535 TA1538	NR	spot test, suspension test with TA1530	0-11.5 µmol/ plate	none	+ + -	There was a dose-related increase in the number of revertants/plate in TA1530 at ≤11.5 µmol/plate.	Brem et al., 1974
Reverse mutation	S. typhimurium TA98 TA100 TA1535	NR	vapor phase closed system	1.6-8.1 µmol/ plate	±S-9 ±S-9 ±S-9	- +/+ +/+	Dose-related increase in the numbers of revertants/plate in TA100 and TA1535.	Barber et al., 1981
Reverse mutation	S. typhimurium TA100	>99.5%	liquid incubation	0-4 mM	±GSH	-	There was a slight dose-related increase in the number of revertants/plate both in the presence and absence of GSH, but the increase was not ≥2-fold above control.	van Bladeren et al., 1981
Reverse mutation	S. typhimurium TA100	>99.5%	liquid incubation	0-4 mM	+GSH and S-100	+	A dramatic dose-related increase in the number of revertants/plate occurred when the S-100 (100,000 g supernatant) from rat liver homogenate was added.	van Bladeren et al., 1981
DNA repair	Escherichia coli pol A+, pol A-	NR	spot test	10 µg/disc	none	+	NC	Brem et al., 1974
CHO/ HGPRT*	Chinese hamster ovary cells	NR	cell culture	0-0.8 mM	±S-9	+/+	The compound was 4-fold more mutagenic in the presence of S-9.	Tan and Hsie, 1981
DNA damage	male B6C3F1 mice - liver DNA	>99.9%	i.p. injection	0, 0.5, 0.75 or 1.0 mmol/kg	NA	+	~9-25% decrease in percent of double stranded DNA (i.e. increase in single strand breaks).	Storer and Conolly, 1982

*Hypoxanthine-guanine phosphoribosyl transferase

NA = not applicable

NC = no comment

NR = not reported

van Bladeren et al. (1981). No appreciable increase in the number of revertants/plate was observed when S. typhimurium strain TA100 was incubated with 1-bromo-2-chloroethane, either in the presence or absence of GSH. When the S-100 fraction containing the cytosolic enzyme, GSH-transferase, was added, however, there was a marked dose-related increase in the number of revertants/plate.

1-Bromo-2-chloroethane was positive for DNA repair when tested without metabolic activation in Escherichia coli strains pol A^+ and pol A^- (Brem et al., 1974). The addition of the S-9 fraction resulted in a 4-fold increased mutagenicity in the CHO/HGPRT mammalian gene mutation assay (Tan and Hsie, 1981). A dose-related decrease in the percentage of double-stranded (i.e. an increase in single strand breaks) DNA was observed in the livers of $B6C3F_1$ male mice sacrificed 4 hours following i.p. injection of 1-bromo-2-chloroethane at 0, 0.5, 0.75 or 1.0 mmol/kg (Storer and Conolly, 1983).

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of bromochloroethanes were not located in the available literature cited in the Appendix.

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding the reproductive effects of bromochloroethanes were not located in the available literature cited in the Appendix.

5.5. CHRONIC TOXICITY

Pertinent data regarding the chronic or subchronic toxicity of bromochloroethanes were not located in the available literature cited in the Appendix.

5.6. OTHER RELEVANT INFORMATION

The oral LD_{50} for 1-bromo-2-chloroethane in rats is 64 mg/kg (NIOSH, 1984). Valade (1957) determined that inhalation of several alkyl halides by

dogs, rats and guinea pigs led to CNS disruption as evidenced by ataxia. An LC_{50} for 1-bromo-2-chloroethane of 15-25 g/m³ for 30 minutes was reported.

In order to assess the acute hepatotoxicity and nephrotoxicity of 1-bromo-2-chloroethane, male $B6C3F_1$ mice were dosed intraperitoneally with the compound in corn oil at 0, 0.75, 1.0 or 1.5 mmol/kg and were sacrificed at 24 hours (Storer and Conolly, 1983). Liver and kidneys were removed and weighed, and blood was drawn for determination of serum enzyme and BUN levels. As indicated in Table 5-2, only at 1.5 mmol/kg were there significant changes from control in the parameters examined.

Moody et al. (1980, 1981) observed a substantial decrease in hepatic cytochrome P-450 in young adult male S-D rats treated by gavage with a single dose of 1-bromo-2-chloroethane at 250 mg/kg, and attempted to correlate this with altered fatty acid content of the hepatic microsomes. The relative content of palmitic, oleic and linoleic acids was increased and the relative content of stearic, arachidonic and docosahexanoic acids was decreased. Treatment with 1-bromo-2-chloroethane reduced cytochrome P-450 levels to 57% of control levels (0.57 vs. 1.0ΔOD/mg protein). Decreases in cytochromes P-450 and b_5 showed high degrees of correlation with decreased arachidonic acid and increased linoleic acid. Treatment with bromochloroethane resulted in elevated liver-to-body weight ratios, an ~7% decrease in microsomal RNA, decreased NADPH-cytochrome c reductase, decreased cytochrome P-450, decreased cytochrome b_5, decreased microsomal phospholipid, and decreased diene conjugates in rat liver microsomes (Moody et al., 1981). Ivanetich et al. (1981) investigated the influence of 1,2-dibromo-1,2-dichloroethane on the redox behavior of hepatic microsomal cytochrome b_5 *in vitro*. Hepatic microsomes were prepared from rats fed a high

TABLE 5-2

Acute Toxicity of 1-Bromo-2-Chloroethane in Male B6C3F$_1$ Mice[a,b]

Compound	Dose (mmol/kg)	Liver Weight[c]	Serum IDH[d]	Serum GPT[d]	Kidney Weight[c]	BUN[e]	Mortality
Control	0	4.54±0.25	13.5±5.9	5.2±1.2	1.41±0.08	12.2±1.6	0/13
BCE	0.75	4.64±0.23	10.3±1.8	5.4±0.9	1.39±0.07	11.8±2.1	0/5
BCE	1.0	4.98±0.29	12.0±1.8	6.0±0.8	1.44±0.05	12.0±1.4	0/5
BCE	1.5	6.13±0.93[f]	1117.3±1167.0[f]	787.9±1071.6[f]	1.63±0.13[f]	19.3±10.5[f]	5/11

[a]Source: Storer and Conolly, 1983

[b]Results are mean ± S.D.

[c]Organ weight/100 g body weight

[d]Data are given in international units/ℓ of serum at 25°C. IDH, L-iditol dehydrogenase (EC 1.1.1.14) GPT, glutamic-pyruvic transaminase (EC 2.6.1.1)

[e]mg urea nitrogen/100 mℓ serum

[f]Significantly different from control ($p<0.05$).

carbohydrate diet to elevate levels of stearate desaturase, or fasted to decrease levels of this enzyme. For microsomes from rats with elevated levels of stearate desaturase, the rate constant for the reoxidation of cytochrome b_5 was increased, and the magnitude of this decrease was reduced by KCN. For microsomes from fasted rats, reoxidation was diminished and cyanide sensitivity was eliminated. The activity of microsomal NADH and NADPH-cytochrome c reductase was not affected. No inhibition of stearoyl CoA metabolism was observed. It was concluded that 1,2-dibromo-1,2-dichloroethane stimulated hepatic microsomal electron transfer from NADH via cytochrome b_5 by interacting with cytochrome P-450 and with stearate desaturase.

6. AQUATIC TOXICITY

Pertinent data regarding the toxicity of any bromochloroethanes on aquatic organisms were not located in the available literature cited in the Appendix.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

Pertinent guidelines and standards, including EPA ambient water and air quality criteria, drinking water standards, FAO/WHO ADIs, EPA or FDA tolerances for raw agricultural commodities or foods, and ACGIH, NIOSH or OSHA occupational exposure limits were not loated in the available literature cited in the Appendix.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of bromochloroethane compounds were not located in the available literature cited in the Appendix.

8. RISK ASSESSMENT

The lack of carcinogenicity and chronic toxicity data for bromochloroethanes precludes the derivation of the q_1^* and ADI. It should be noted that related haloalkanes have been associated with the development of liver tumors, squamous cell carcinomas of the forestomach and adenomas and carcinomas of the upper respiratory tract (IARC, 1979).

Mutagenicity studies of 1-bromo-2-chloroethane were available and indicate that the compound was positive for reverse mutation in several strains of Salmonella typhimurium, for DNA repair in Escherichia coli, for mutation in the CHO/HGPRT system and for DNA damage in mice in vivo (see Table 5-1). Metabolic activation enhances the mutagenic response.

Although chronic and subchronic data are lacking, single i.p. injection of male $B6C3F_1$ male mice resulted in significant elevations in liver and kidney weight, serum L-iditol dehydrogenase, SGPT, BUN and mortality at 1.5 mmol/kg, but not at 1.0 or 0.75 mmol/kg (Storer and Conolly, 1983) (see Table 5-2).

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY

Subchronic and chronic studies of bromochloroethanes were not located in the available literature cited in the Appendix; therefore, derivation of the RQ is precluded (Table 9-1).

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

Studies of the carcinogenic potential of bromochloroethanes were not located in the available literature cited in the Appendix; therefore, the derivation of the potency factor is precluded. According to the IARC classification, these compounds are Class 3 chemicals; that is, the group of chemicals cannot be classified as to its carcinogenicity for humans. Given the inadequacy of the animal date and the absence of epidemiological studies, the cancer assessment group of U.S. EPA under their proposed carcinogenic classification scheme, rank bromochloroethanes as group C chemicals. Group C correlates with IARC Class 3. It should be noted, however, that several related halogenated alkanes have been associated with the induction of liver tumors, squamous cell carcinomas of the forestomach, and upper respiratory adenomas and carcinomas in rodents (IARC, 1979).

TABLE 9-1

Bromochloroethanes

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:

Dose:

Effect:

Reference:

RV_d:

RV_e:

Composite Score:

RQ: Data are not sufficient for deriving an RQ.

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APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of the following:

CA SEARCH (Files 308, 309, 310, 311, 320
TOXLINE
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP

These searches were conducted in July, 1984. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981, 1982, 1983). Cincinnati, OH. 486 p.

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In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

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